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  - ☐ Fee Attached
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  - ☐ Affidavits/declaration(s)
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- ☐ Certified Copy of Priority Document(s)
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  - ☐ Reply to Missing Parts under 37 CFR 1.52 or 1.53
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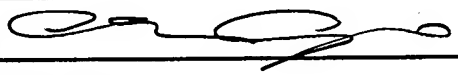
Signature			
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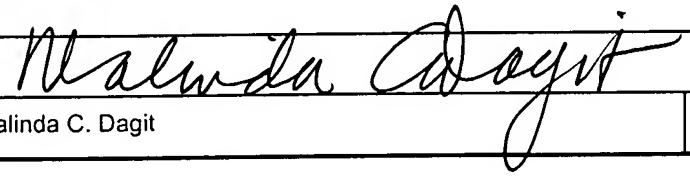
Signature			
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TOWNSEND and TOWNSEND and CREW LLP

By: Malinda Adagot

PATENT
Attorney Docket No.: 018512-005920US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Timothy James Jegla

Application No.: 10/815,297

Filed: March 31, 2004

For: KV10.1, A NOVEL VOLTAGE-GATED POTASSIUM CHANNEL FROM HUMAN BRAIN

Customer No.: 20350

Confirmation No. No. 8561

Examiner: CHERNYSHEV, Olga N.

Technology Center/Art Unit: 1649

APPELLANT'S REPLY BRIEF UNDER 37 C.F.R. §41.41

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Sir:

This brief is filed pursuant to 37 C.F.R. §41.41, in response to the Examiner's Answer mailed January 17, 2008. A Request for an Oral Hearing is NOT filed.

I. The Maintained Rejections and Evidence of Record

Claims 12-14 and 16-18 stand rejected under 35 U.S.C. §101 for alleged lack of patentable utility and under 35 U.S.C. §112, first paragraph, for alleged lack of enablement due to lack of utility. Appellant respectfully traverses these rejections and argues that they are improper, because the Examiner has neither established a *prima facie* showing of lack of utility and nor rebutted Dr. Krafte's declaration regarding the utility of the claimed invention.

Independent claim 12 of this application is drawn to an isolated polypeptide comprising an alpha subunit of a Kv potassium channel, referred to as a Kv10.1 subunit. The polypeptide forms, with at least one additional Kv alpha subunit, a voltage-gated Kv potassium channel, and comprises an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:3. The remaining claims all directly depend from claim 12. The specification asserts a specific and substantial utility of the claimed invention: Kv10.1 is a subunit of a voltage-gated potassium channel and can be used to screen for modulators of voltage-gated potassium channels comprising a Kv10 subunit. Because of the known involvement of Kv channels in regulating various biological processes such as neuronal integration and cell proliferation and also because of the expression pattern of Kv10.1 in the brain, spinal cord, prostate, and retina, it is asserted that these modulators are useful for treating disorders of the central nervous system and for modulating male fertility. During prosecution of this application, Appellant has offered explanations and evidence to support this asserted utility, including a declaration by Dr. Douglas Krafte and three publications by Wu *et al.*, Singh *et al.*, and Wickenden *et al.* (presented as Exhibits B-D of Dr. Krafte's declaration).

In contrast, the Examiner relies on no evidence to raise and maintain the utility and utility-based enablement rejections. See page 3, lines 1-2, of the Examiner's Answer.

II. The Examiner Has Not Provided Objective Reasons Sufficient to Overcome the Presumption of Patentable Utility

According to MPEP §2107, an applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement of 35 U.S.C. §101. To properly make and sustain a utility rejection, an examiner must carry the initial burden to make a *prima facie* showing of lack of utility by providing a detailed explanation with specific evidence or reasoning to support the conclusion of lack of utility.

In the Examiner's Answer, however, the Examiner continues to argue repeatedly that the utility rejection and utility-based enablement rejection are proper, because Appellant has provided no evidence to support the asserted utility. See, *e.g.*, the last paragraph on page 3; the last paragraph on page 5; line 10 on page 6; the last paragraph on page 9; and the last paragraph on page 18. To further require evidence as proof of utility after a patent applicant has already made a clear assertion of utility is inconsistent with the standards for utility assessment set forth in the MPEP and the prevailing case law. It is the Examiner, not Appellant, who bears the initial burden to justify the conclusion regarding utility.

Although without the initial burden, Appellant has nonetheless offered as evidence Dr. Krafte's declaration and accompanying publications to establish that the asserted utility is specific, substantial, and credible to an ordinarily skilled artisan. Dr. Krafte attests in his declaration that, given the general knowledge of Kv channels and the specific expression pattern of Kv10.1, a person of ordinary skill in the art would find the asserted utility credible. He further explains that an ion channel can be a therapeutic target even though the ion channel itself does not cause the disease or condition being treated. In the Examiner's Answer, however, the Examiner argues that the declaration merely reflects the general knowledge in the art and is in agreement with the Examiner's position (*i.e.*, K^+ channels are involved in a large variety of biological processes). Appellant sees no inconsistency between the general knowledge in the art (including the

diversity of biological processes in which K^+ channels participate) and the asserted utility of the claimed invention in this application.

On page 13 of the Examiner's Answer, the Examiner states that the declaration provides no reasonable explanation as to why one skilled in the art would recognize the Kv10.1 channel being specifically associated with CNS disorders, vision disorders, or male fertility conditions. This statement is simply incorrect, as Dr. Krafte clearly attests in paragraph 6 of his declaration:

> Several subfamilies of the Kv potassium channel family have previously been identified. These potassium channels are indicated in signal transduction during various biological processes such as neuronal integration, cardiac pacemaking, muscle contraction, hormone secretion, cell volume regulation, lymphocyte differentiation, and cell proliferation. Given this knowledge and the specific expression of Kv10.1 in the CNS, male reproductive organs, and retina, one of ordinary skill in the art would recognize the Kv10 channel as a therapeutic target for treating CNS or vision disorders or for regulating male infertility.

In the same paragraph of the declaration, Dr. Krafte refers to the Wu *et al.* reference as further confirmation that Kv10.1 indeed plays a role in various vision disorders. Thus, Appellant has established, by way of Dr. Krafte's statement and also by way of evidence (the Wu *et al.* publication), a credible, specific, and substantial asserted utility, which the Examiner has not sufficiently rebutted.

The Examiner contends that the USPTO need not accept as fact any and all statements in a patent application, unless one of ordinary skill in the art would find such statements credible in view of the evidence of record. See the last paragraph on page 16 and the first paragraph on page 17 of the Examiner's Answer. Appellant completely agrees with the Examiner on this point. Indeed, the evidence of record shows data of Kv10.1 channel activity, expression pattern, and Dr. Krafte's declaration in which Dr. Krafte, a person of ordinary skill in the art, explains the indication of the data

presented in the specification and attests that he finds the asserted utility credible. Thus, the instant case appears to be just the situation where the Examiner should accept the asserted utility as fact.

No Identification of a Specific Disease or Condition Is Required

The Examiner argues that the claimed invention lacks utility because "there is no evidence presented in the specification that a protein of the instant invention naturally forms a heteromultimeric voltage gated potassium channel in combination with Kv2.2 or that such a combination has an established biological role in a particular disease, disorder or physiological process which one would wish to manipulate for a desired clinical effect." See the paragraph bridging pages 3 and 4 of the Examiner's Answer. Appellant respectfully disagrees.

First of all, the specification does disclose "a specific biological role" for the Kv10.1 protein: a subunit of a voltage-gated potassium channel, and "a particular disease" or "disorder" for which a desired clinical benefit can be gained via manipulation of the protein: CNS disorders, vision disorders, and male fertility conditions.

Secondly, *the Revised Interim Utility Guidelines Training Materials* ("the *Utility Guidelines*") promulgated by the USPTO impose no requirement of identifying a treatable disease for utility purpose in certain context. More specifically, Example 8 of the *Utility Guidelines* describes a scenario in which a compound A is disclosed to inhibit enzyme XYZ, a well known enzyme, *in vitro*. The specification states that the compound A can be used to treat diseases caused or exacerbated by enzyme XYZ, but ***names no such diseases***. Claim 1 is directed to compound A. Claim 2 is directed to a method of treating a disease caused or exacerbated by enzyme XYZ consisting of administering an effective amount of compound A to a patient. In the subsequent analysis, claim 2 is deemed to be insufficiently supported by a real world context of use, because neither the specification nor the art of record discloses any disease or conditions caused or exacerbated by enzyme XYZ and therefore, the asserted utility is seen as a method of

treating an unspecified and undisclosed disease or condition, which does not define a "real world" context of use. Claim 1, however, is regarded as having utility because claim 1 is directed to a compound that inhibits an enzyme and enzymes have well established utility in the art, *i.e.*, catalyzing certain reactions, even though no specific diseases are identified. Because the pending claims in this application are not drawn to the therapeutic use of a Kv10.1 channel modulator, identification of a particular disease is not required.

Furthermore, as explained by Dr. Krafte in paragraph 8 of his declaration, it is not necessary that the instant application disclose a disease or physiological condition that is caused by anomaly in the claimed Kv10.1 polypeptide in order to meet the utility requirement.

The Instant Case Is Not Analogous to Brenner v. Manson

The Examiner argues on page 4 of the Examiner's Answer that the claimed invention in this application lacks utility because "[t]he instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q 689 (Sup. Ct. 1996)." Appellant cannot agree.

In *Brenner v. Manson*, the claim in question is directed to a process to produce a steroid that is among a class of a structurally similar steroids being tested for anti-tumor activity. the Supreme Court found that the process, as well as the steroid it produces, is without utility under 35 U.S.C. §101. The Court agreed with the PTO's reasoning in raising the utility rejection, which is, despite the reference to the purported anti-tumor activity of an adjacent homologue, the patent applicant did not establish a sufficient likelihood that the steroid produced by his process would have similar activity, because "minor changes in the structure of a steroid may produce profound changes in its biological activity." 148 USPQ at 694.

The fact pattern of the present application is, however, very much distinct from that of *Brenner v. Manson*. To begin with, the asserted utility in the present

application does not solely rely upon the purported utility of an analog or homolog of the claimed Kv10.1 subunit. The recognition of Kv10.1 as a voltage-gated potassium channel subunit is based on the protein's primary amino acid sequence, in view of the well-known structural characteristics of potassium channels of the Kv family. The asserted utility of the a Kv10.1 channel is based on the protein express profile and the biological activity of the Kv potassium channel family. More importantly, the center piece of the *Brenner v. Manson* decision, namely the "great unknown unpredictability of compounds in that field," 148 USPQ at 694, does not exist in the instant application. Quite to the contrary, potassium channels have been the focus of intense research effort for the past few decades, and a vast amount of knowledge has been accumulated with regard to the classification of these channels and the structural and functional features attributable to each family or subfamily. In other words, as soon as the coding sequence and amino acid sequence of a new potassium channel are identified, a skilled artisan would recognize with virtual certainty as to (1) which family or subfamily this new channel belongs to and (2) the biological role of this new channel. There is simply no "great unknown unpredictability" in the field.

Because of these important factual distinctions, Applicants contend that the instant case is not analogous to *Brenner v. Manson*. The Supreme Court decision in *Brenner v. Manson* therefore should not be mechanically applied in this application.

The Claimed Kv10.1 Polypeptide Meets the Requirement under the Utility Guidelines

Beginning on page 15 of the Examiner's Answer, the Examiner argues that the fact pattern of this application and Example 8 of the *Utility Guidelines*" are not analogous; instead, the Examiner takes the position that the Kv10.1 channel protein is analogous to the "orphan receptor" in Example 12 of the *Utility Guidelines*. Applicants respectfully disagree with the Examiner's analysis.

First, the Examiner's approach to distinguish enzymes and ion channels solely based on what biological process they mediate is rigid and unreasonable. Enzymes

are proteins that belong to defined classes that catalyze certain chemical reactions. Ion channels are proteins that belong to defined classes that regulate ion passage across a cellular membrane. From the perspective of their roles, enzymes and ion channels are very similar in nature because they both facilitate a well-defined process that serves a larger biological/physiological purpose. To artificially classify "enzymes" as proteins that "provide a well-defined and particular benefit to the public" and therefore have utility and "ion channels" as proteins that provide no benefit to the public and therefore have no utility therefore has no merits scientifically.

Second, the Examiner argues that the claimed Kv10.1 polypeptide is akin to the "orphan receptor" of Example 12 of the *Utility Guidelines* and therefore should be held without utility. Appellant contends that the Kv10.1 polypeptide shares far more similarities with the enzyme of Example 8 and has little in common with the "orphan receptor" of Example 12. This because an ion channel protein is known to participate in a defined process with known and measurable outcome, much like an enzyme, whereas an "orphan receptor" is not known to participate in any particular biological process or produce any detectable results.

Accordingly, Applicants submit that analysis of the pending claims under the *Utility Guidelines* supports a conclusion of sufficient utility, as no valid reasons have been provided to indicate the contrary.

The Examiner's Refusal to Consider Post-Filing Information for Utility Purpose is Erroneous

Appellant reiterates that the Examiner is wrong in her refusal to consider post-filing publications for the sole purpose of confirming a utility already explicitly asserted in the specification. As Appellant has pointed out in the Appeal Brief, this application clearly presents an asserted utility of the claimed invention: Kv10 channels can be used for identifying Kv10 channel modulators, which in turn can be used for therapeutic agents for treating CNS, vision, or male fertility disorders. None of the post-

filing references are cited to establish a patentable utility not previously set forth; these references are used only to **confirm** a utility that is already fully described and expressly asserted in the specification. The Examiner's treatment of post-filing publications that are cited for the sole purpose of confirming previously asserted utility is directly and completely contrary to the USPTO's long-standing practice.

In regard to the Examiner's comment on the relevance of the Singh reference to the present application (see the second full paragraph on page 17 of the Examiner's Answer), Appellant notes that Dr. Krafte refers to the Singh reference, which describes the involvement of another Kv channel, KCNV2, in epilepsy, and uses it as an example to convey the point that, because Kv channels are known to play a role in certain CNS disorders, one of skill in the art would find the asserted utility of Kv10.1 credible.

In summary, the Examiner has not carried the initial burden to establish a *prima facie* case of lack of patentable utility; the Examiner has not rebutted the evidence presented by way of Dr. Krafte's declaration and accompanying publications on utility; and the Examiner has relied on flawed reasoning in assessing the utility question of this invention. As such, Appellant contends that the utility rejection and the utility-based enablement rejection are improper and respectfully request their reversal.

III. The Utility Rejection Contradicts the Allowance of the Parent Application

The immediate parent of this application, USSN 09/833,466, has issued as U.S. Patent No. 6,727,353. Because the present application claims a Kv10.1 polypeptide, and the '353 patent claims a Kv10.1 nucleic acid, Appellant contends that maintaining the utility rejection (and the utility-based enablement rejection) in this application would create a direct and irreconcilable contradiction in the USPTO's utility practice. In response, the Examiner argues that treatment of a claim in one application is immaterial to the treatment of a similar claim in another application and cites *In re Wertheim*, 191

USPQ 90 (CCPA 1976), to support her position. See the bridging paragraph on pages 17-18 of the Examiner's Answer.

Appellant does not agree with this overly broad reading of the case law. Upon a close review of *In re Wertheim* as well as *In re Giolito and Hofmann*, 188 USPQ 645 (CCPA 1976), which is cited in *In re Wertheim*, Appellant recognizes that the two cases stand for the position of permitting inconsistent treatment of similar claims in ***completely unrelated, different*** applications. In stark contrast, the '353 patent and the instant application are ***completely identical*** in their specification and the claims are directed to two aspects of the same subject matter: a Kv10.1 nucleic acid and its encoded protein. Because of this important distinction, it is inappropriate to apply the holding of *In re Wertheim* or *In re Giolito and Hofmann* to the present application.

IV. Conclusion

In view of the foregoing, Appellant believes that the utility rejection and utility-based enablement rejection are improper, reversal of these rejections are therefore respectfully requested.

Respectfully submitted,

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